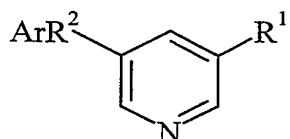


We Claim:

1. A method for treating a disorder remedied by antagonism of mGlu5 receptors in a patient which comprises administering to a patient in need thereof an effective amount of a compound of formula 1:



(1)

wherein

- 10 Ar is phenyl or naphthyl each of which may be substituted by one or more C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₅ acyl, halo, amino, nitro, cyano, hydroxy, C₁-C₅ acylamino, C₁-C₄ alkylsulfonylamino, mono-, di- or trifluorinated C₁-C₃ alkyl, substituents which may be the same or different and may bear a CONH₂, CONHCH₃, CON(CH₃)₂, CO₂H, CO₂CH₃, OCF₃, CH₂NHCOCH₃, CH₂NH₂, CH₂N(CH₃)₂, CH₂CN, CH₂OH,
- 15 CH₂NHSO₂CH₃, CH₂N(CH₃)(CH₂)₂CN, CH₂N(CH₃)CH(CH₃)₂, CH₂NHCH(CH₃)₂, CH₂NH(CH₂)₂CH₃, CH₂NHCO₂R⁴, CH₂NHCH₂CH₃, CH₂NHCH₃, NHCOC(CH₃)₂, or N(S(O)₂CH₃)₂ substituent;

R¹ is hydrogen, halo, R⁴, CN, C(NO₂)R³, C(NO-R⁴)R³, (CH₂)₂CO₂R⁴, (CH₂)_nOR³, COR³, CF₃, SR⁴, S(O)R⁴, S(O)₂R⁴, COCH₂CO₂R³, NHSO₂R⁴, NHCOR³,

20 C(NOR³)NH₂, CH₂OCOR³, (CH₂)_nNH₂, CON(CH₃)₂, (CH₂)_nNHCO₂R⁴, CO₂R³, CONH₂, CSNH₂, C(NH)NHOR³, (CH₂)_nN(CH₃)₂, or CONHNHCOR³;

R² is 1,2-ethenediyl or 1,2-ethynediyl;

R³ is hydrogen or C₁-C₄ alkyl;

R⁴ is C₁-C₄ alkyl; and

25 n is 0, 1, 2, 3 or 4;

or a pharmaceutically acceptable salt thereof; or an N-oxide thereof.

2. A method as claimed in Claim 1 wherein

Ar is C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₅acyl, halo, amino, nitro, cyano, hydroxy, C₁-C₅ acylamino, C₁-C₄ alkylsulfonylamino or mono-, di- or trifluorinated C₁-C₃ alkyl; and

5 R¹ is hydrogen, halo, R⁴, CN, C(NO_H)R³, C(NOR⁴)R³, (CH₂)₂CO₂-R⁴, OR³, COR³ or CF₃.

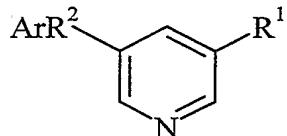
3. The method of any one of Claims 1 or 2 wherein the disorder is pain or

10 anxiety.

4. The method of any one of Claims 1-3 wherein the patient is a human.

5. A compound of formula 1:

15



(1)

wherein

Ar is phenyl or naphthyl each of which may be substituted by one or more C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₅ acyl, halo, amino, nitro, cyano, hydroxy, C₁-C₅ acylamino, C₁-C₄ alkylsulfonylamino, mono-, di- or trifluorinated C₁-C₃ alkyl, substituents which may be the same or different and may bear a CONH₂, CONHCH₃, CON(CH₃)₂, CO₂H, CO₂CH₃, OCF₃, CH₂NHCOCH₃, CH₂NH₂, CH₂N(CH₃)₂, CH₂CN, CH₂OH, CH₂NHSO₂CH₃, CH₂N(CH₃)(CH₂)₂CN, CH₂N(CH₃)CH(CH₃)₂, CH₂NHCH(CH₃)₂, CH₂NH(CH₂)₂CH₃, CH₂NHCO₂R⁴, CH₂NHCH₂CH₃, CH₂NHCH₃, NHCOC(CH₃)₂, or 25 N(S(O)₂CH₃)₂ substituent;

R¹ is hydrogen, halo, R⁴, CN, C(NO_H)R³, C(NOR⁴)R³, (CH₂)₂CO₂R⁴, (CH₂)_n OR³, COR³, CF₃, SR⁴, S(O)R⁴, S(O)₂R⁴, COCH₂CO₂R³, NHSO₂R⁴, NHCOR³,

C(NOR³)NH₂, CH₂OCOR³, (CH₂)_nNH₂, CON(CH₃)₂, (CH₂)_nNHCO₂R⁴, CO₂R³,

CONH₂, CSNH₂, C(NH)NHOR³, (CH₂)_nN(CH₃)₂, or CONHNHCOR³;

R² is 1,2-ethenediyl or 1,2-ethynediyl;

R³ is hydrogen or C₁-C₄ alkyl;

5 R⁴ is C₁-C₄ alkyl; and

n is 0, 1, 2, 3 or 4;

or a pharmaceutically acceptable salt thereof; or an N-oxide thereof; provided that the compound is other than 5-phenylethynyl-nictinonitrile.

10 6. The compound of Claim 5 wherein n is 0 or 1.

7. The compound of any one of Claims 5 or 6 wherein Ar is phenyl substituted by one or more halo, C₁-C₄ alkyl, CN, C₁-C₄ alkoxy, CF₃, NO₂, NH₂, OH, COCH₃, substituents which may be the same or different and may bear a CONH₂, CONHCH₃, CON(CH₃)₂, CO₂H, CO₂CH₃, OCF₃, CH₂NHCOCH₃, CH₂NH₂, CH₂N(CH₃)₂, CH₂CN, CH₂OH, CH₂NHSO₂CH₃, CH₂N(CH₃)(CH₂)₂CN, CH₂N(CH₃)CH(CH₃)₂, CH₂NHCH(CH₃)₂, CH₂NH(CH₂)₂CH₃, CH₂NHCO₂C(CH₃)₃, CH₂NHCH₂CH₃, CH₂NHCH₃ or NHCOC(CH₃)₂ substituent.

20 8. The compound of any one of Claims 5-7 wherein halo is fluoro, iodo, choro or bromo; alkyl is methyl, ethyl, propyl, isopropyl or isobutyl; and alkoxy is methoxy.

25 9. The compound of any one of Claims 5-8 wherein Ar is 2-chlorophenyl, 3-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 3,4-dimethylphenyl, 3,5-dimethylphenyl, 2,4-dimethylphenyl, 2,5-dimethylphenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-chlorophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 3,4,5-trifluorophenyl,

30 3-bromophenyl, 3-nitrophenyl, 3-trifluoromethylphenyl, 3-aminophenyl,

3-chloro-4-fluorophenyl, 3-hydroxyphenyl, 3-acetylphenyl, 5-chloro-2-methoxyphenyl,
3-chloro-4-methoxyphenyl, 3-hydroxy-4-fluorophenyl, 3-methoxy-4-fluorophenyl,

3-ethoxy-4-fluorophenyl, 3-isopropoxy-4-fluorophenyl, 3-isopropylphenyl,
3-ethylphenyl, 3-methyl-4-fluorophenyl, 3-trifluoromethyl-4-fluorophenyl,

5 3-cyano-4-fluorophenyl, 3-amino-4-fluorophenyl,

3-trifluoromethyl-4-fluorophenyl, 3-chloro-4-fluorophenyl,

3-nitro-4-fluorophenyl, 3-aminocarbonyl-4-fluorophenyl,

3-N-methylaminocarbonyl-4-fluorophenyl,

3-N,N-dimethylaminocarbonyl-4-fluorophenyl, 3-carboxyl-4-fluorophenyl,

10 3-methoxycarbonyl-4-fluorophenyl, 3-acetylaminomethyl-4-fluorophenyl,

3-methysulfonylaminomethyl-4-fluorophenyl,

3-pivaloylaminomethyl-4-fluorophenyl, 3-trifluoromethoxyphenyl,

3-aminomethyl-4-fluorophenyl, 3-dimethylaminomethyl-4-fluorophenyl,

3-cyanomethyl-4-fluorophenyl, 4-fluoro-3-hydroxymethylphenyl,

15 3-{[(2-cyanoethyl)-methylamino]-methyl}-4-fluorophenyl,

4-fluoro-3-[(isopropylmethylamino)-methyl]phenyl,

4-fluoro-3-isopropylaminomethylphenyl, 4-fluoro-3-propylaminomethylphenyl,

3-ethylaminomethyl-4-fluorophenyl, 4-fluoro-3-methyl aminomethylphenyl,

3-isobutyryl amino-4-fluorophenyl or 3-aminophenyl.

20

10. The compound of any one of Claims 5-9 wherein R¹ is hydrogen, bromo, iodoo, fluoro, chloro, C(NO_H)R³, C(NO-R⁴)R³, methyl, CN, CH₂CO₂R⁴, (CH₂)_nOR³, COR³, CF₃, SR⁴, S(O)R⁴, S(O)₂R⁴, COCH₂CO₂R³, NHS(O)₂R³, NHCOR³, CH₂OC(O)R³, (CH²)_nNH₂, CON(CH₃)₂, (CH₂)_nNHCO₂R⁴, CO₂R³, CONH₂, CSNH₂, C(NH)NHOR³, (CH₂)_nN(CH₃)₂ or CONHNHCOR³.

25

11. The compound of any one of Claims 5-10 wherein R³ is hydrogen, methyl, ethyl or *t*-butyl.

12. The compound of Claim 5 wherein

Ar is phenyl or napthyl each of which may be substituted by C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₅ acyl, halo, amino, nitro, cyano, hydroxy, C₁-C₅ acylamino, C₁-C₄ alkylsulfonylamino or mono-, di- or trifluorinated C₁-C₃ alkyl; and

5 R¹ is hydrogen, halo, R⁴, CN, C(NO_H)R³, C(NOR⁴)R³
(CH)₂CO₂R⁴, OR³, COR³ or CF₃.

13. The compound of formula I as claimed in any one of Claims 5-12 wherein

10 R¹ is CN, iodo, chloro, methyl or COR³.

14. The compound of formula I as claimed in any one of Claims 5-13 wherein

R¹ is CN.

15 15. The compound of formula I as claimed in any one of Claims 5-14 wherein

R² is 1,2-ethynediyl.

16. The compound of formula 1 as claimed in any one of Claims 5-15 wherein C₁-C₄ alkyl is methyl.

20

17. The compound of formula 1 as claimed in any one of Claims 5-16 wherein R³ is methyl.

18. A compound of formula 1 as claimed in any one of a Claims 5-16 wherein

25 R³ is hydrogen.

19. The compound of any one of Claims 5-18 wherein substituted Ar is substituted phenyl.

30

20. The compound of any one of Claims 5-6, 8 or 10-18 wherein Ar is phenyl.

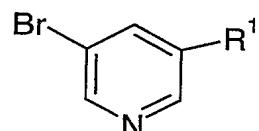
21. A compound of claim 5 which is:

5-(4-Fluorophenylethynyl)-nicotinonitrile, 5-(3-Cyanophenylethynyl)-nicotinonitrile or 5-(3,4-difluorophenylethynyl)-nicotinonitrile.

5

22. A process for preparing a compound of formula 1 (or a pharmaceutically acceptable salt thereof) as provided in any one of the above Claims 5-21 which comprises:

- 10 (a) for a compound of formula 1 in which R^2 is 1,2-ethenediyl, reacting with a compound of formula II

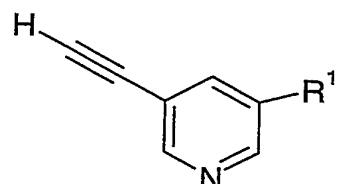


(II)

with a compound of formula Ar-CHCH₂ in a Heck coupling;

15

- (b) for a compound of formula 1 in which R^2 is alkynyl, reacting with a compound of formula III



(III)

20 in a Sonogashira coupling with a compound of formula Ar-I or Ar-Br in a suitable solvent;

whereafter, for any of the above procedures, when a pharmaceutically acceptable salt of a compound of formula 1 is required, it is obtained by reacting the basic form of such a compound of formula 1 with an acid affording a physiologically acceptable

counterion, or, for a compound of formula 1 which bears an acidic moiety, reacting the acidic form of such a compound of formula 1 with a base which affords a pharmaceutically acceptable cation, or by any other conventional procedure; and wherein, unless more specifically described, the value of R¹, Ar and R² are as defined in Claim 5.

5

23. A pharmaceutical composition comprising in association with a pharmaceutically acceptable carrier, diluent or excipient, a compound of formula 1 (or a pharmaceutically acceptable salt thereof) as provided in any one of the above Claims 5-21.

10

24. A compound of formula 1 as claimed in Claim 1 for use in therapy.

25. Use of compound of formula 1 as claimed in Claim 1 for the manufacture of a medicament for treating a disorder remedied by antagonism of mGlu5 receptors in a
15 patient.